AR 201-12549b17

ROBUST SUMMARY
ALKYL SULFIDE CATETGORY
CAS # 68511-50-2
HEALTH ELEMENTS: REPEATED DOSE TOXICITY

Test Substance	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "Chemical Description of Alkyl Sulfide Category" in HERTG's Test Plan for Alkyl Sulfide Category.
Method	
Method/Guideline followed	None cited
Test Type	21 Day Repeated Dose Dermal Toxicity Study
GLP (Y/N)	N
Year (Study Performed)	1979
Species	Rabbit
Strain	New Zealand White
Route of administration	Dermal to shaved skin of backs and sides
Duration of test	21 days
Doses/concentration levels	40 animals tested: 3 treatment groups (7M/3F, 8M/2F, 6M/4F), 1 untreated control (5M/5F) Group 1: 140 mg/kg/day undiluted test material Group 2: 560 mg/kg/day undiluted test material Group 3: 2240 mg/kg/day undiluted test material
Sex	Male and female
Exposure period	
Frequency of treatment	
Control group and treatment	1 untreated control (5M/5F)
Post exposure observation period	
Statistical methods	None cited.
Remarks field for test conditions	Age of animals at initiation: Not specified following at least 2 weeks acclimation. Study was designed to evaluate local and systemic effects of test material when applied dermally. Methyl propene derivative was applied to the shaved backs and sides (approximately 10% of the body surface) of 3 groups of 10 N.Z. White rabbits 5 days per week for 3 weeks at dose levels of 140, 560 or 2240 mg/kg/day of undiluted test material on the same test schedule. The animals were fitted with plastic collars to inhibit ingestion of the test material, which was left uncovered on the skin and not removed prior to the next dose. One untreated shaved control group of 10 animals was included in the study. Assessments for local and systemic effects included twice daily

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	(morning and afternoon) clinical observations, skin irritation scoring 5 days per week, weekly body weights, hematology, serum chemistry and urinalysis at pretest and termination, and gross necropsy evaluations at study termination.
Results	
Remarks	All rabbits survived the duration of the test. Body weight changes were within expected ranges and comparable for all groups. Rabbits in all groups had lethargy, ptosis, G.I. disturbances, nasal and ocular discharges and respiratory distress, all more often in the second and third weeks with no discernible pattern of response. Skin responses included slight to moderate erythema and very slight to slight edema during Week 1 for all treated groups. During Week 2 responses in all treated groups were moderate to severe erythema with additional signs of cracked skin, bleeding and discoloration. Edema was slight at the lowest dose and slight to moderate at the higher doses. During Week 3 all treated groups had severe erythema with cracked and bleeding skin, eschar and discoloration and edema was slight to moderate. No irritation was observed in the control group. Urinalysis values were normal in all groups. Several individual and isolated hematological and serum chemistry values were out of expected range but with no discernible treatment related changes in the mean values for all groups. At necropsy, sporadic occurrences of dark lungs and liver, red and bloated intestines, pale kidney or small or gray spleen were noted with no relationship to treatment. Epithelial hyperplasia of the treated skin was observed in all rabbits with the treated groups exhibiting slightly more severe grades of hyperplasia than the control group. The rabbits were grouped by sex at the start of the study. At necropsy six errors in sexing were discovered which resulted in uneven sex distribution within the groups. Since there were no apparent effect differences between the sexes, the study is not considered to be compromised. With no discernable pattern of response in both test and control groups, observed clinical signs are considered to be related to handling. The occurrence of hyperplasia in all groups suggests a relationship to clipping rather to test material administration. However, *in-life* dermal observations revealed severe erythema responses in all treated rabbits and none in the sham treated control group.

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Conclusions	A NOAEL was not established in this study. The LOEL for clinical signs and systemic toxicity was 140 mg/kg/day dermal exposure for 3 weeks. No minimally irritating concentration was identified by this study.
Data Quality	Reliable with restrictions. Animal age and organ weight data were not included in the report. The test site was not occluded following test material application.
References	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
Other	Updated: 12-28-99